

## WEST Search History

DATE: Tuesday, September 04, 2007

Hide?	<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>
		<i>DB=PGPB,USPT; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L7	L4 and (@AD<20021024 or @RLAD<20020124 or @PRAD<20021024)	2
<input type="checkbox"/>	L6	L4 and (Zeldis.in. or Faleck.in. or Manning.in.)	1
<input type="checkbox"/>	L5	L4 and (celgene.as.)	5
<input type="checkbox"/>	L4	L3 and ((complex regional pain syndrome) or (reflex sympathetic dystrophy))	15
<input type="checkbox"/>	L3	514/417.icls. or 514/417.ccls.	358

END OF SEARCH HISTORY

FILE 'REGISTRY' ENTERED AT 13:08:42 ON 04 SEP 2007  
L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 3 S L1 FAM FULL

FILE 'STNGUIDE' ENTERED AT 13:09:42 ON 04 SEP 2007

FILE 'HCAPLUS' ENTERED AT 13:11:42 ON 04 SEP 2007  
L4 17 S L3/THU  
L5 285 S (COMPLEX REGIONAL PAIN SYNDROME) OR (REFLEX SYMPATHETIC DYSTR  
L6 3827 S (NEUROPATHIC PAIN)  
L7 0 S L4 AND L5  
L8 1 S L4 AND L6  
L9 0 S L7 AND (PY<2003 OR AY<2003 OR PRY<2003)  
L10 0 S L8 AND (PY<2003 OR AY<2003 OR PRY<2003)

FILE 'STNGUIDE' ENTERED AT 13:11:55 ON 04 SEP 2007

FILE 'HCAPLUS' ENTERED AT 13:12:09 ON 04 SEP 2007

FILE 'STNGUIDE' ENTERED AT 13:12:09 ON 04 SEP 2007

FILE 'HCAPLUS' ENTERED AT 13:12:43 ON 04 SEP 2007  
L11 4 S L4 AND PAIN

=> file registry  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 13:08:42 ON 04 SEP 2007  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 SEP 2007 HIGHEST RN 945955-20-4  
DICTIONARY FILE UPDATES: 3 SEP 2007 HIGHEST RN 945955-20-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

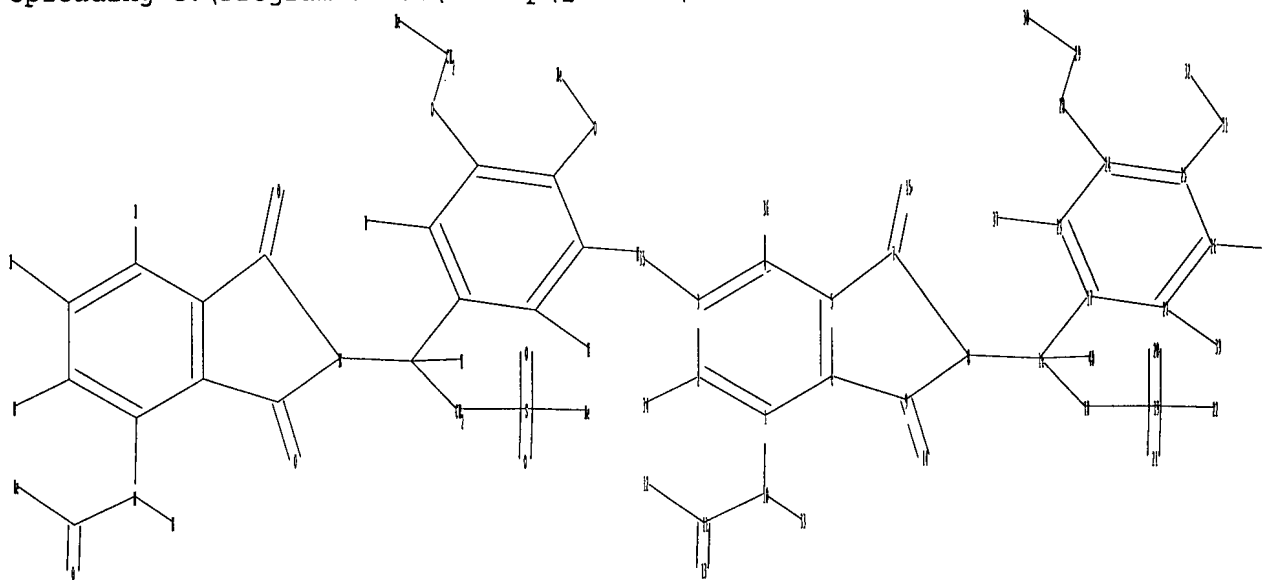
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>  
Uploading C:\Program Files\Stnexp\Queries\10693722elected.str



chain nodes :  
10 11 12 13 14 15 16 18 19 20 21 22 28 29 30 31 32 33 34 35 36  
37 38 39 40  
ring nodes :  
1 2 3 4 5 6 7 8 9 17 23 24 25 26 27  
chain bonds :  
1-10 2-34 3-35 4-36 7-15 8-16 9-14 10-11 10-33 11-12 11-13 16-17 16-18  
16-40 18-19 19-20 19-21 19-22 23-37 24-28 25-31 26-38 27-39 28-29 29-30  
31-32

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 17-23 17-27 23-24 24-25 25-26  
26-27

exact/norm bonds :

1-10 5-7 6-9 7-8 7-15 8-9 8-16 9-14 10-11 11-13 19-20 19-21 24-28 25-31

exact bonds :

2-34 3-35 4-36 10-33 11-12 16-17 16-18 16-40 18-19 19-22 23-37 26-38  
27-39 28-29 29-30 31-32

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 17-23 17-27 23-24 24-25 25-26 26-27

Match level :

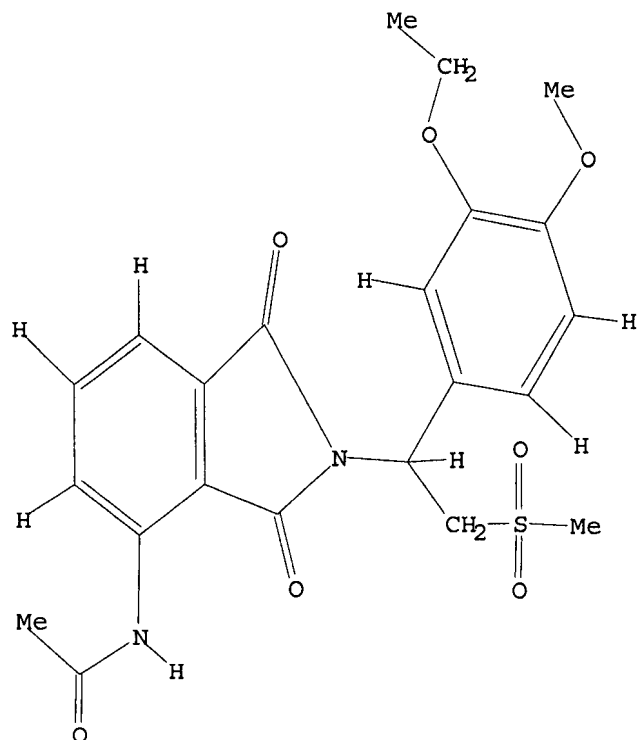
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11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:CLASS  
19:CLASS 20:CLASS  
21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS 29:CLASS  
30:CLASS 31:CLASS  
32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS  
40:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 13:09:21 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 5 TO 234  
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 fam full

FULL SEARCH INITIATED 13:09:29 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 66 TO ITERATE

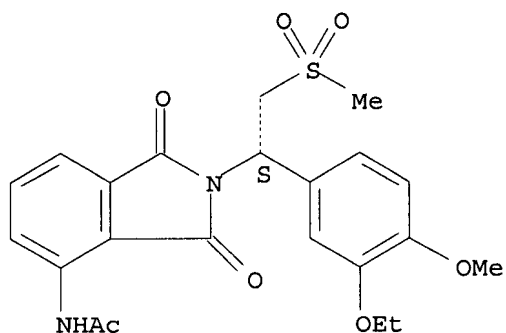
100.0% PROCESSED 66 ITERATIONS 3 ANSWERS  
SEARCH TIME: 00.00.01

L3 3 SEA FAM FUL L1

=> d l3 scan

L3 3 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN Acetamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(  
(methylsulfonyl)ethyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]-  
MF C22 H24 N2 O7 S

Absolute stereochemistry. Rotation (+).

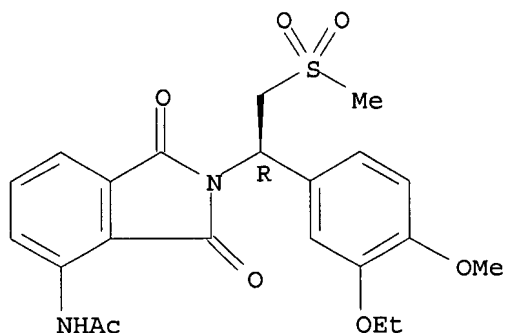


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

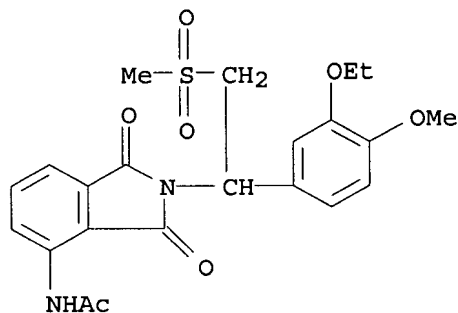
L3 3 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(  
(methylsulfonyl)ethyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]-  
MF C22 H24 N2 O7 S

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L3 3 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
 IN Acetamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-  
 dihydro-1,3-dioxo-1H-isoindol-4-yl]-  
 MF C22 H24 N2 O7 S



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> file stnguide  
 COST IN U.S. DOLLARS  
 FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
68.15	68.36

FILE 'STNGUIDE' ENTERED AT 13:09:42 ON 04 SEP 2007  
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FILE CONTAINS CURRENT INFORMATION.  
 LAST RELOADED: Aug 31, 2007 (20070831/UP).

=> file hcplus  
 COST IN U.S. DOLLARS  
 FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
0.18	68.54

FILE 'HCAPLUS' ENTERED AT 13:11:42 ON 04 SEP 2007  
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FILE COVERS 1907 - 4 Sep 2007 VOL 147 ISS 11  
FILE LAST UPDATED: 3 Sep 2007 (20070903/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13/thu

```
          17 L3
        930166 THU/RL
L4          17 L3/THU
           (L3 (L) THU/RL)
```

=> s (complex regional pain syndrome) or (reflex sympathetic dystrophy)

```
        1359500 COMPLEX
          69518 REGIONAL
          53372 PAIN
        130648 SYNDROME
          127 COMPLEX REGIONAL PAIN SYNDROME
            (COMPLEX (W) REGIONAL (W) PAIN (W) SYNDROME)
          25547 REFLEX
          40356 SYMPATHETIC
          13389 DYSTROPHY
            182 REFLEX SYMPATHETIC DYSTROPHY
              (REFLEX (W) SYMPATHETIC (W) DYSTROPHY)
L5          285 (COMPLEX REGIONAL PAIN SYNDROME) OR (REFLEX SYMPATHETIC DYSTROPH
              Y)
```

=> s (neuropathic pain)

```
          4915 NEUROPATHIC
          53372 PAIN
L6          3827 (NEUROPATHIC PAIN)
              (NEUROPATHIC (W) PAIN)
```

=> s 14 and 15

```
L7          0 L4 AND L5
```

=> s 14 and 16

```
L8          1 L4 AND L6
```

=> s 17 and (PY<2003 or AY<2003 or PRY<2003)

22887930 PY<2003  
4458517 AY<2003  
3937141 PRY<2003  
L9 0 L7 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> s l8 and (PY<2003 or AY<2003 or PRY<2003)

22887930 PY<2003  
4458517 AY<2003  
3937141 PRY<2003  
L10 0 L8 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.60	71.14

FILE 'STNGUIDE' ENTERED AT 13:11:55 ON 04 SEP 2007  
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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Aug 31, 2007 (20070831/UP).

=> d l8 ti abs bib  
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Composition comprising fumaric acid ester for treatment of an autoimmune  
and/or inflammatory disorder and related conditions  
AB The present invention relates to compns., kits and methods for  
administration of a first component of fumaric acid ester(s), or a  
pharmaceutically acceptable salt thereof, and a second component which is  
a substance that reduces or eliminates flushing.  
AN 2007:439616 HCAPLUS <<LOGINID::20070904>>  
DN 146:448435  
TI Composition comprising fumaric acid ester for treatment of an autoimmune  
and/or inflammatory disorder and related conditions  
IN Nilsson, Henrik  
PA Aditech Pharma AB, Swed.  
SO PCT Int. Appl., 48pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007042035	A2	20070419	WO 2006-DK563	20061006
WO 2007042035	A3	20070614		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,			



KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA  
 WO 2006037342 A2 20060413 WO 2005-DK648 20051007  
 WO 2006037342 A3 20060720

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,  
 NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,  
 SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,  
 YU, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM

PRAI WO 2005-DK648 A 20051007  
 DK 2006-511 A 20060407  
 US 2006-744458P P 20060407  
 DK 2004-1546 A 20041008  
 DK 2004-1736 A 20041110  
 DK 2005-211 A 20050211  
 DK 2005-419 A 20050323  
 US 2005-691513P P 20050616

=> file hcaplus		
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	76.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'HCAPLUS' ENTERED AT 13:12:43 ON 04 SEP 2007  
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FILE COVERS 1907 - 4 Sep 2007 VOL 147 ISS 11  
 FILE LAST UPDATED: 3 Sep 2007 (20070903/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4 and pain

53372 PAIN  
 L11 4 L4 AND PAIN

=> file stnguide

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY  
2.60

TOTAL  
SESSION  
79.29

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE  
ENTRY  
0.00

TOTAL  
SESSION  
-0.78

CA SUBSCRIBER PRICE

FILE 'STNGUIDE' ENTERED AT 13:12:44 ON 04 SEP 2007  
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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Aug 31, 2007 (20070831/UP).

=> d l11 1-4 ti

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Composition comprising fumaric acid ester for treatment of an autoimmune  
and/or inflammatory disorder and related conditions

L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Preparation of substituted phenethyl sulfones and methods of reducing  
TNF $\alpha$  levels

L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-  
acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting  
TNF- $\alpha$  production and PDE4 activity

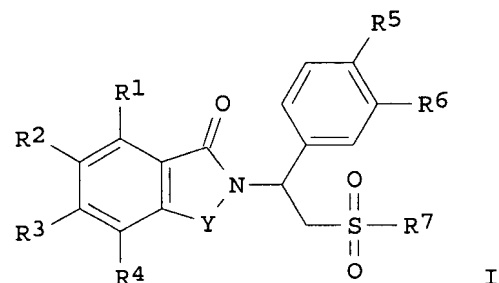
L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Use of (-)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-  
acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting  
TNF- $\alpha$  production and PDE4 activity

=> d l11 2-4 ti abs bib

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
TI Preparation of substituted phenethyl sulfones and methods of reducing  
TNF $\alpha$  levels

GI



AB The title compds. I [Y = CO, CH<sub>2</sub>, SO<sub>2</sub>, CH<sub>2</sub>C(O); R<sub>1</sub>-R<sub>4</sub> = H, halo, alkyl, alkoxy, etc.; R<sub>5</sub>, R<sub>6</sub> = H, alkyl, alkoxy, CN, etc.; R<sub>7</sub> = OH, alkyl, Ph, etc.], useful for reducing TNF $\alpha$  levels and treating inflammatory and autoimmune diseases, were prepared and formulated. E.g., a 2-step synthesis of 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]isoindolin-1-one, starting from di-Me sulfone and 3-ethoxy-4-methoxybenzaldehyde, was given.

AN 2006:425851 HCAPLUS <<LOGINID::20070904>>

DN 147:189068

TI Preparation of substituted phenethyl sulfones and methods of reducing TNF $\alpha$  levels

IN Man, Hon-Wah; Muller, George W.

PA Celgene Corporation, USA

SO Aust. Pat. Appl., 53 pp.

CODEN: AUXXCM

DT Patent

LA English

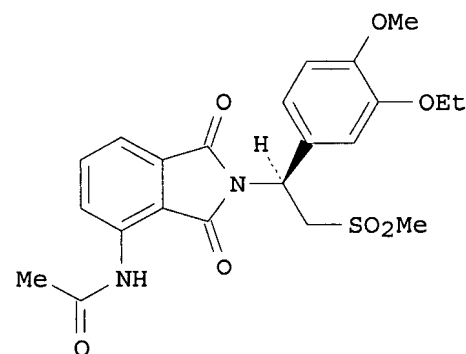
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AU 2006200033	A1	20060202	AU 2006-200033	20060106
	AU 2003203681	A1	20030703	AU 2003-203681	20030409
PRAI	AU 2003-203681	A3	20030409		
	AU 2000-14472	A3	19991019		
	WO 1999-US24376	W	19991019		

L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminisoindoline-1,3-dione and compositions thereof for inhibiting TNF- $\alpha$  production and PDE4 activity

GI



AB The invention discloses stereomerically pure (S)-2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminisoindoline-1,3-dione (+)-I, substantially free of its (-)-isomer, and prodrugs, metabolites, polymorphs, salts, solvates, hydrates, and clathrates thereof. Methods of using and pharmaceutical compns. comprising (+)-I for treating and/or preventing disorders ameliorated by the reduction of levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) or the inhibition of phosphodiesterase IV (PDE4) are also disclosed. Examples include the synthesis and resolution of (+)-I, thirteen bioassays, an aqueous solubility study, and three formulations. For instance, 3-nitrophthalic acid was hydrogenated using 10% Pd/C in EtOH to give the amine (84%), which was condensed with Ac<sub>2</sub>O to afford 3-acetamidophthalic anhydride (61%). Reaction of the phthalic anhydride with 1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethylamine to give I (59%), followed by resolution with N-acetyl-L-leucine in MeOH provided (+)-I

(90% recovery, 98.4% ee). The latter inhibited LPS-induced TNF- $\alpha$  production by human whole blood and PDE4 activity with IC50 values of 294 nM and 73.5 nM, resp. (+)-I showed >500-fold to >40,000-fold selectivity for PDE4 over PDE1, PDE2, PDE3, PDE5, and PDE6. In addition, (+)-I suppressed LPS-induced lung neutrophilia in conscious ferrets with an ED50 of 0.8 mg/kg. Thus, (+)-I and its pharmaceutical compns. are useful for treating and/or preventing cancer, depression, and a variety of allergic, inflammatory, and autoimmune disorders (no data).

AN 2003:777583 HCAPLUS <<LOGINID::20070904>>

DN 139:296870

TI Use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting TNF- $\alpha$  production and PDE4 activity

IN Schafer, Peter H.; Muller, George W.; Man, Hon-Wah; Ge, Chuansheng

PA Celgene Corporation, USA

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

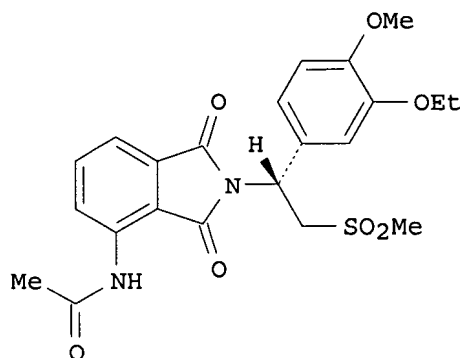
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
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	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	CA 2479666	A1	20031002	CA 2003-2479666	20030320	
	AU 2003224729	A1	20031008	AU 2003-224729	20030320	
	EP 1485087	A1	20041215	EP 2003-721414	20030320	
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	CN 1652772	A	20050810	CN 2003-811093	20030320	
	JP 2005525386	T	20050825	JP 2003-577877	20030320	
	NZ 535798	A	20060428	NZ 2003-535798	20030320	
	CN 1965823	A	20070523	CN 2006-10137407	20030320	
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PRAI	US 2002-366515P	P	20020320			
	US 2003-438450P	P	20030107			
	CN 2003-811093	A3	20030320			
	WO 2003-US8738	W	20030320			

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Use of (-)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting TNF- $\alpha$  production and PDE4 activity

GI



I

AB The invention discloses stereomerically pure (R)-2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione (-)-I, substantially free of its (+)-isomer, and prodrugs, metabolites, polymorphs, salts, solvates, hydrates, and clathrates thereof. Methods of using and pharmaceutical compns. comprising (-)-I for treating and/or preventing disorders ameliorated by the reduction of levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) or the inhibition of phosphodiesterase IV (PDE4) are also disclosed. Examples include the synthesis and resolution of (-)-I, seven bioassays, an aqueous solubility study, and three formulations.

For

instance, 3-nitrophthalic acid was hydrogenated using 10% Pd/C in EtOH to give the amine (84%), which was condensed with Ac2O to afford 3-acetamidophthalic anhydride (61%). Reaction of the phthalic anhydride with 1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethylamine to give I (59%), followed by resolution with N-acetyl-D-leucine in MeOH provided (-)-I (90% recovery, 98.4% ee). The latter inhibited LPS-induced TNF- $\alpha$  production by human whole blood and PDE4 activity with IC50 values of 371 nM and 611 nM, resp. (-)-I showed >45-fold to >39,000-fold selectivity for PDE4 over PDE1, PDE2, PDE3, PDE5, and PDE6. Thus, (-)-I and its pharmaceutical compns. are useful for treating and/or preventing cancer, depression, and a variety of allergic, inflammatory, and autoimmune disorders (no data).

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TI Use of (-)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting TNF- $\alpha$  production and PDE4 activity

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PA Celgene Corporation, USA

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DT Patent

LA English

FAN.CNT 1

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PI	WO 2003080048	A1	20031002	WO 2003-US8737	20030320
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

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RE.CNT 3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT